

Early congenital syphilis still occurs

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SUMMARY Seven cases of early congenital syphilis have been recorded in the past 10 years in the Mersey Regional Health Authority. Antenatal serology was initially negative in five mothers, who were either incubating or acquired the infection later, and treatment had probably failed in two women given erythromycin for syphilis during pregnancy. Serology should be repeated later in pregnancy in those at high risk. Social factors that define this group include women who book for antenatal care late in pregnancy, have a past history of sexually transmitted disease, and have multiple consorts. Clinical signs in the infant such as failure to thrive, hepatosplenomegaly, symmetrical rash, rhinitis, and osteochondritis should alert the clinician to the possibility of congenital syphilis.

Adequate management of mother and baby requires close liaison between the genitourinary physician, microbiologist, obstetrician, and paediatrician. Penicillin remains the treatment of choice.

Early congenital syphilis is totally preventable but still occurs in Britain and the USA,¹ and in the latter, in recent years, it is clear that the increase in the number of reported cases parallels a striking increase in primary and secondary syphilis in women. In the UK, during the 11 years 1973 to 1983, 122 cases of early congenital syphilis (in children less than 2 years of age) were recorded and annual figures varied, with wide fluctuations between English health regions. This is despite a high degree of organisation in our national maternity services and sophisticated supportive specialities. A patient with congenital syphilis presented to us in 1984, and this prompted us to conduct a wider search of our laboratory and other records for further cases in this region. We have studied the clinical, serological, and socioeconomic data on the affected babies in Merseyside, and discuss some of the reasons for the failure to prevent this disease in the community.

Materials and methods

Cases of congenital syphilis recorded in Merseyside between 1974 and 1982 were extracted from the computer register of the Mersey Regional Health Authority. Cross checking of laboratory records at Liverpool Public Health Laboratory and Manchester Central Serology Laboratory, as well as clinical

records of the genitourinary medicine clinics in the region, was also undertaken, and figures for 1983 to 1984 were acquired from these sources.

Details of socioeconomic status, disease classification, and treatment in the mothers were obtained from the genitourinary medicine clinic records (where available) and from the infants' case notes. Clinical, radiological, serological, and treatment details of the infants were obtained from paediatric and laboratory records. The number of cases of congenital syphilis in the English regions (1973 to 1983) was obtained from the Department of Health and Social Security, and the total for the UK (1973 to 1983) was obtained from the Communicable Diseases Surveillance Centre.

In this region sera from all pregnant women at their first antenatal clinic visit are routinely screened by the Liverpool Blood Transfusion Service. Screening was previously done by the automated reagin test but more recently the venereal disease research laboratory test and the *Treponema pallidum* haemagglutination test have been used. Any sera with positive or doubtful results are then referred, as are blood samples from all other patients in the region, to the Liverpool Public Health Laboratory where rapid plasma reagin and *Treponema pallidum* haemagglutination tests are performed routinely, and fluorescent treponemal antibody (absorbed) and IgM tests are performed when appropriate.

Some cross boundary specimen referral occurs with the Manchester Central Serology Laboratory, where additional tests (for example cardiolipin Wassermann reaction, venereal disease research laboratory, and fluorescent treponemal antibody (absorbed) IgM tests) are undertaken.

Results

In the Mersey region the average annual population in the period 1974–84 was 2·466 million and the average annual number of births (live and still births) was 31 312. In the same period, a total of seven cases of early congenital syphilis (less than 2 years of age) were identified in this region—one case each in years 1978, 1981–4 inclusive and two in 1979. A total of 122 cases were reported in the UK between 1973 and 1983 (figures for 1984 were unavailable at the time of writing) with a range of eight to 17 per year except in 1983 when only one case was reported.

Mothers. Maternal age ranged from 19 to 27 years—four women were single and three were married: two were multigravida and five were primigravida. One woman had been treated for gonorrhoea and another currently had perianal warts. Five mothers were diagnosed as having early latent syphilis, one had secondary syphilis, and the stage of infection could not be classified in the last mother because of persistent defaulting from follow up.

Five mothers had a negative venereal disease research laboratory test at the first visit to the antenatal clinic. Four of these women had first attended the antenatal clinic after the 20th week of pregnancy; two attended as late as the third trimester. These five women subsequently had positive venereal disease research laboratory, rapid plasma reagin, and treponema pallidum haemagglutination tests which were undertaken after the diagnosis of congenital syphilis was made in their babies. Two women admitted to intercourse with different consorts subsequent to the first antenatal visit.

One of the remaining two women was treated abroad with erythromycin (250 mg orally four times a day for 10 days) during her pregnancy after she was found to have positive serology. One mother who presented at 26 weeks' gestation had positive serological tests but defaulted until the 36th week and then had a course of erythromycin base (250 mg orally four times a day for two weeks) because of alleged penicillin allergy.

Consorts. Two of the consorts were seamen, one was a prisoner, three were tradesmen, and one was

of unknown occupation. One man was treated abroad and another was admitted to hospital with lymphadenopathy and was found to have positive syphilis serology as part of a diagnostic screen. This led to detection of the disease in his child who had symptoms of irritability, hepatosplenomegaly, and a rash.

Infants. There were three boys and four girls. The birthweights varied from 2·7 to 3·5 kgs in those infants born at term. One child was born at 33 weeks' gestation and weighed 1·8 kg. Of the six infants diagnosed after birth, age at presentation varied from 2 to 16 weeks. Three of the weights

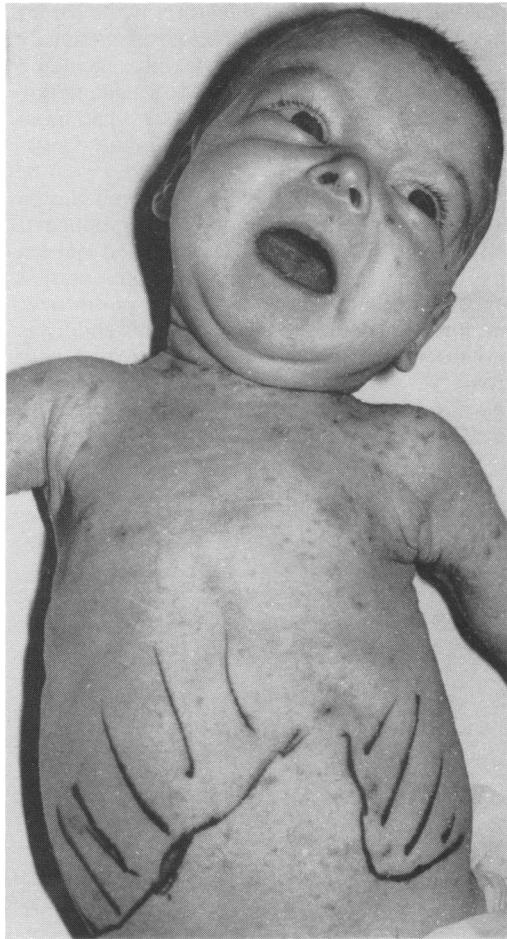


Fig. 1 Hepatosplenomegaly (enlargement indicated) and maculopapular rash in a 3 month old infant presenting with congenital syphilis. Note evidence of failure to thrive—redundant axillary skin folds.

Table *Frequency of clinical features in early congenital syphilis*

Hepatosplenomegaly	6/7
Maculopapular/exfoliative rash	4/7
Nasal discharge	2/7
Skeletal involvement (periostitis/Wimberger's sign)	2/7
Jaundice	1/7
Failure to thrive (admission weight <third centile)	3/5*

*Only 5 admission weights recorded: one neonate was diagnosed at birth.

recorded in five children on hospital admission were below the third centile. One child, born to the mother with early latent syphilis who was treated with erythromycin at 36 weeks' gestation, was diagnosed on cord serology.

The frequency of the clinical features in the babies is shown in the Table. Six had hepatosplenomegaly (Fig. 1), four had dermatological features including maculopapular rash (Fig. 1) and desquamating erythema of palms and soles (Fig. 2), two had nasal discharge, and two had radiological changes consistent with syphilis (Fig. 3).

Five of the seven infants had a raised rapid plasma reagin titre on admission. Fluorescent treponemal antibody (absorbed) IgM test was carried out on only five babies; four were positive at presentation and one, on whom serial tests were performed, became positive at 10 weeks of age. This child was born to the second mother who was treated with erythromycin. Three of six infants in whom haemoglobin was estimated were anaemic at presentation, their haemoglobin concentrations ranging from 6.6



Fig. 3 *Metaphyseal defects in upper medial tibial borders (Wimberger's sign).*

to 9.7 g/dl. Only three of seven had serum immunoglobulin tests performed and all had a raised IgM concentration. Four of the seven had liver function tests carried out, and all of these had raised serum glutamic oxaloacetic and pyruvic transaminase activities; but only two had a raised total serum bilirubin concentration of which more than 10% was conjugated.

The treatment records of the infants showed that a variety of penicillin regimens had been used. The preparations had included crystalline penicillin, aqueous procaine penicillin, triplopen (a combination of benethamine penicillin, procaine penicillin, and penicillin G sodium), and procaine penicillin with aluminium monostearate. The total doses,



Fig. 2 *Desquamating erythema of palms and soles in infant with congenital syphilis.*

however, and the duration of treatment were adequate and exceeded those recommended by the World Health Organisation² in all cases.

In the follow up period, four infants have shown no sequelae at 12 months, 15 months, 18 months, and 3½ years of age. Two children have only been seen on one occasion since when they have defaulted from follow up. One child, who was treated at birth, died at 2½ months of age as a cot death. Detailed serial serological follow up in one infant is shown in Fig. 4. It can be seen that the raised plasma rapid reagin value started to fall two and a half months after treatment, eventually becoming negative nine months later. The *Treponema pallidum* haemagglutination test was positive at a high dilution until seven months after treatment, when the

titre began to fall considerably. The fluorescent treponemal antibody (absorbed) test, initially strongly positive, was only weakly reactive 24 months after treatment.

Discussion

Congenital syphilis is not a disease of yesteryear. That it still occurs today and should be considered in neonatal and paediatric practice is illustrated by these seven cases.

The number of cases of early congenital syphilis in the UK between 1973 and 1982 has ranged between eight and 17 per year with a mean of 12, but it seems that only one case was recorded in 1983. The reason for this is uncertain, but may be due to under reporting at this stage. In the USA, in the period 1981–3 (inclusive), the mean annual figure was 159 (at less than 1 year of age), and although the occurrence of primary and secondary syphilis among women increased by 15% in the same period, the number of cases detected through perinatal testing increased to a lesser degree.³ Furthermore, in the USA, 80% of women with primary and secondary syphilis were in the reproductive period of their life.³

In England and Wales (1973–82) some four health regions accounted for 62% of the cases of congenital syphilis (South East Thames 22%, North West Thames 18%, Yorkshire 12%, South West Thames 10% (Department of Health and Social Security)). The Mersey Region accounted for only 4.5%; however, it is also worth noting that during 1984 there were 13 pregnant women with positive serology (excluding biological, false-positive results), in the Mersey Region—the highest figure recorded in the past five years.

In the USA high risk factors identified for early congenital syphilis were inadequate antenatal care and ethnic origin.⁴ In our series all mothers had antenatal care, but only one mother presented before 24 weeks' gestation. Antenatal syphilis serology screening has been standard practice in the UK, and although not a requirement in some American States,¹ a recent review article suggests that some obstetricians in the UK may also doubt the value of such screening in view of the low incidence of syphilis.⁵ If one considers purely economic grounds alone, however, there is still a strong argument for continuing to screen routinely for syphilis in pregnancy.⁶ In our series, antenatal serological tests were positive in two mothers but negative in five (in one as late as 32 weeks' gestation). These mothers were either incubating syphilis or acquired it later in pregnancy (three women admitted to intercourse late in pregnancy—one whose husband was later

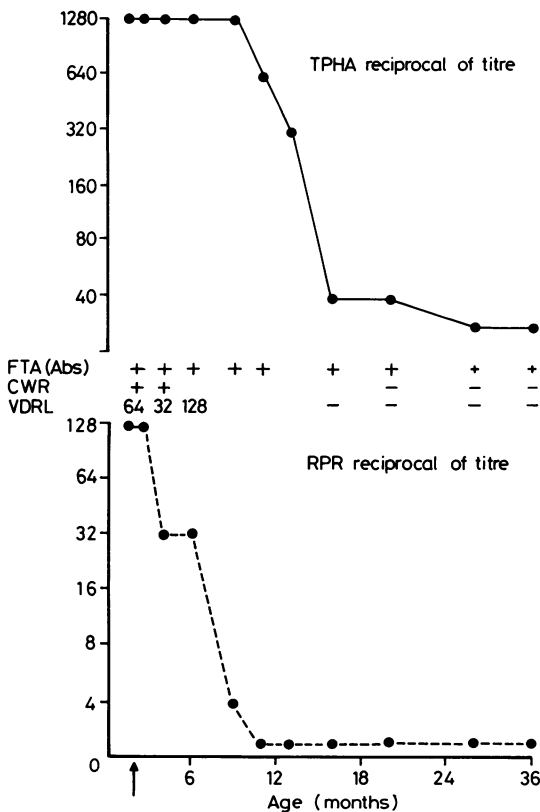


Fig. 4 Detailed serological follow up of infant 5. Results expressed as reciprocal of titre for rapid plasma reagin (RPR), *Treponema pallidum* haemagglutination (TPHA), and venereal disease research laboratory (VDRL). Penicillin treatment was started at ↑.

FTA (Abs)=fluorescent treponemal antibody (absorbed) test.
CWR=cardiolipin Wasserman reaction.

found to be infected and two whose multiple consorts were untraceable). It has also been suggested that serological tests for syphilis should be repeated late in pregnancy in those mothers with a past history of sexually transmitted disease.⁷

One of our mothers had been treated previously for gonorrhoea and another had a history of vulval warts. We would strongly advocate repeat serological testing of the high risk pregnant patient later in pregnancy. Occupation of consort and marital status of the mother may also identify risk factors. Two of the known consorts were seamen and one was an inmate of a nearby prison. Four of our seven mothers were single. Ethnic origin, which was highly relevant in the reports from the USA,⁴ was of no importance in our mothers. Perhaps the higher ethnic incidence in American negroes and hispanics is a consequence of poorer antenatal care in these socially disadvantaged groups.

The stage of maternal syphilis is important in determining the outcome of pregnancy. For example when the mother has untreated primary or secondary disease, infectivity is virtually 100%, but in late maternal syphilis fetal infection is uncommon.⁷ Five of the mothers had early latent syphilis (duration of infection less than two years) and one had secondary syphilis. In our series, despite antenatal diagnosis, transplacental transmission of the disease occurred in two instances, probably because of the use of inappropriate antibiotics or treatment failures, or both.

At birth, abnormal clinical findings were not detected on routine examination of any of our babies. Although only one neonate was of low birthweight (less than 2.5 kg) a further two babies showed evidence of intrauterine growth retardation (weight less than 10th centile for gestational age). The six infants diagnosed after birth were admitted to hospital with 'non-specific' symptoms—fever, irritability, poor feeding, failure to thrive, or skin rashes. All six had hepatosplenomegaly of a moderate degree. It is interesting to note the association of serosanguinous nasal discharge and gross skeletal involvement in one of our babies and minimal periosteal reaction in another at 6 weeks of age.

Clearly, the diagnosis of early congenital syphilis in the first months of life demands clinical vigilance and investigation by appropriate serological tests. The relative merits of the latter have given rise to much debate, particularly the value of the fluorescent treponemal antibody (absorbed) IgM test.⁸⁻¹⁰ Although this test was positive in five of our babies, it took 10 weeks to become so in one. In view of the possibility of materno-fetal transfer of antibodies (excluding IgM) and in the absence of dark field positive lesions, rising titres for rapid plasma reagin

or venereal disease research laboratory tests in the child should be sought to confirm active disease. Borobio *et al*¹¹ reported nine cases of congenital syphilis in which serological diagnosis was based on a positive fluorescent treponemal antibody (absorbed) IgM test combined with high concentrations of serum IgM and a negative result on latex testing (a reason for false positivity). In our series, total IgM was measured in only three infants but was raised in all.

Examination of cerebrospinal fluid should be undertaken routinely in all infants with early congenital syphilis, since this will determine the nature and duration of treatment. Follow up surveillance should be continued for at least two years in babies to ensure clinical and serological cure. Adequate treatment and serological follow up of affected mothers during pregnancy is also imperative.

Congenital syphilis will invariably be prevented if the mother is treated adequately with penicillin, and treatment is completed at least two weeks before delivery.¹² A history of penicillin allergy in the mother should be critically questioned since the efficacy of erythromycin, which diffuses poorly into fetal circulation, is not well established.^{2 13} In our series, both babies born to mothers treated with erythromycin were affected, and other workers have also reported the failure of erythromycin to cure syphilis in a pregnant woman, probably because the base does not produce adequate serum concentrations.^{13 14}

Because of the lack of uniform treatment in our babies we would endorse the WHO recommendation that in early congenital syphilis procaine or crystalline penicillin G (50 000 U/kg body weight; the latter in two divided doses daily being the preferred treatment if the cerebrospinal fluid is abnormal) should be given intramuscularly daily for 10 days.² Alternatively, benzathine penicillin (50 000 U/kg body weight intramuscularly as a single dose) can be used provided the cerebrospinal fluid is normal (because of its poor penetration across the blood brain barrier).² If the mother was inadequately treated or treated with erythromycin during pregnancy the infant should be given a course of penicillin as recommended above. The indiscriminate or inadvertent use of antibiotics may mask the diagnosis of early congenital syphilis and result in inadequate or partial treatment of this disease. For example, in one of our infants, penicillin was prescribed for bronchiolitis, and moderate hepatosplenomegaly though noted was attributed to diaphragmatic depression and hyperinflation of the lungs. One questions the outcome of early congenital syphilis in this child if the diagnosis had not been established.

This study has shown that close cooperation between the genitourinary physician, microbiologist, obstetrician, and paediatrician is of paramount importance in the management of maternal and early congenital syphilis.

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